

Indicator: Phthalate Exposure (347)

Phthalates are industrial chemicals added to many consumer products such as food packaging, plastics (plastic bags, garden hoses, recreational toys, medical tubing, plastic clothes, etc.), adhesives, detergents, personal-care products (such as soap, shampoo, nail polish, et.), and many others. Exposure can occur through food that has been in contact with phthalate containing packaging as well as direct contact with products that contain phthalates. The health effects of phthalates in humans have not been well studied (CDC, 2003). Acute high dose exposure to Di (2-ethylhexyl) phthalate may be associated with mild gastrointestinal disturbances, nausea and vertigo (EPA, 2005). Chronic exposure may be associated with damage to the liver and testes, cancer, and adverse reproductive effects.

This indicator is based on data collected by the National Health and Nutrition Examination Survey (NHANES). NHANES is a series of surveys conducted by CDC's National Center for Health Statistics (NCHS) that is designed to collect data on the health and nutritional status of the civilian, non-institutionalized U.S. population using a complex, stratified, multistage, probability-cluster design. Beginning in 1999, NHANES became a continuous and annual national survey; biomonitoring for certain environmental chemicals also was implemented. These data are presented here as a baseline with the intent of reporting trends in the future.

What the Data Show

Table 347Phthalate presents the geometric means for urinary concentrations and creatinine-adjusted urinary concentrations of seven selected metabolites of phthalates among a subsample of participants aged six years and older from NHANES 1999-2000. Mono-ethyl phthalate (metabolite for diethyl phthalate, an industrial solvent used in many products including those containing fragrances), mono-butyl phthalate (metabolite for dibutyl phthalate, an industrial solvent used in cosmetics, printing inks, insecticides), mono-benzyl phthalate (metabolite for benzylbutyl phthalate, an industrial solvent used in adhesives, vinyl flooring, and car care products), and mono-2-ethylhexyl phthalate (metabolite for di-2-ethylhexyl phthalate, used to produce flexible plastics) had geometric means of 179 µg/L, 24.6 µg/L, 15.3 µg/L, and 3.4 µg/L, respectively. Mono-cyclohexyl phthalate, mono-n-octyl phthalate, and mono-isononyl phthalate were not measured with sufficient frequency above the limit of detection to calculate a geometric mean.

The geometric mean levels for mono-ethyl phthalate, mono-butyl phthalate, mono-benzyl phthalate, and mon-2-ethylhexyl phthalate among specified demographic subgroups were compared after adjustment for the covariates of race/ethnicity, age, gender, and urinary creatinine. For those aged 6-11 years compared to the older age groups (12-19 years and 20+ years), urinary mono-ethyl phthalate levels were found to be lower, but urinary mono-butyl, mono-benzyl, and mono-2-ethylhexl phthalates were higher (CDC, 2003). Females tended to have a higher level than males for mono-ethyl, mono-butyl, and mono-benzyl phthalates. Non-Hispanic blacks had higher levels of mono-ethyl phthalate than non-Hispanic whites or Mexican Americans.

Indicator Limitations

- NHANES selects a representative sample of the civilian, non-institutionalized population in the United States using a complex, stratified, multistage, probability-cluster design. Beginning in 1999, NHANES became a continuous and annual national survey. With only 2 years of data in NHANES 1999-2000, instead of the 6-years for NHANES III (1988-1994), some differences exist that may limit the underlying data with respect to completeness or representative of coverage.

- The sample size is smaller and the number of geographic units in the sample is more limited. The current 1999-2000 NHANES survey is nationally representative but it is subject to the limits of increased sampling error due to (1) the smaller number of individuals sampled in the annual sample and (2) the smaller number of Primary Sampling Units (PSUs) [see description below] available for each annual sample. Therefore, the sample size for any 1-year period is relatively small, possibly resulting in large variability for U.S. population estimates, especially those for narrowly defined demographic groups or other specific subgroup analyses.
 - For NHANES 1999-2000, the first stage of selection was the PSU-level. The PSUs were defined as single counties. For a few PSUs, the county population was too small and those counties were combined with geographically contiguous counties to form a PSU. The 1999-2000 NHANES sample is selected from a relatively small number of PSUs compared to NHANES III. With a small number of PSUs, variance estimates that account for the complex design may be relatively unstable, a factor which introduces a higher level of uncertainty in the annual estimates.
 - NHANES is designed to increase precision by combining data across calendar years. Because of the relatively small sample size in 1999 and 2000, analytical data for just one or two survey participants may be weighted heavily and greatly influence the mean value reported.
 - The number of geographic sites sampled each year is small and environmental exposures may vary geographically; thus producing environmental exposure estimates by geographic region using the NHANES data set is of limited value.
- Differences in the excretion of various phthalates may be due to differences in either exposure or toxicokinetics. The low detection rates for some of the long alkyl chain phthalates metabolites may be due to significantly less metabolism to the monoester metabolite.
 - It is unknown whether differences between ages, genders, or races/ethnicities represent differences in exposure, body-size relationships, or metabolism.
 - Generally recognized guidelines for urinary levels of these phthalate metabolites have not been established.
 - The measurement of an environmental chemical in a person's blood or urine does not by itself mean that the chemical has caused or will cause harmful effects.

Data Sources

Centers for Disease Control and Prevention. 2003. Second National Report on Human Exposure to Environmental Chemicals. (Accessed November 21, 2004)
<http://www.cdc.gov/exposurereport/2nd/pdf/secondner.pdf>

References

Centers for Disease Control and Prevention. 2003. Second National Report on Human Exposure to Environmental Chemicals. (Accessed November 21, 2004)
<http://www.cdc.gov/exposurereport/2nd/pdf/secondner.pdf>

Environmental Protection Agency. 2005. Consumer Factsheet on : Di(2-ethylhexyl) phthalate. (Accessed March 21, 2005). <http://www.epa.gov/safewater/dwh/c-soc/phthalat.html>

Graphics

Table 347Phthalate. Geometric mean and selected percentiles of selected phthalate metabolite urine concentrations and creatinine-adjusted levels for the United States population, aged 6 years and older, National Health and Nutrition Examination Survey (NHANES), 1999-2000

	Sample Size	Geometric Mean	10 th	25 th	50 th	75 th	90 th
Mono-ethyl phthalate							
µg/L of urine	2536	179.0	28.9	61.4	164.0	450.0	1260.0
µg/g of creatinine*	2536	163.0	33.0	64.7	141.0	360.0	898.0
Mono-butyl phthalate							
µg/L of urine	2541	24.6	5.7	12.6	26.0	51.6	98.6
µg/g of creatinine*	2541	22.4	7.7	12.8	21.9	38.9	68.3
Mono-benzyl phthalate							
µg/L of urine	2541	15.3	2.8	6.9	17.0	35.3	67.1
µg/g of creatinine*	2541	14.0	4.4	7.6	13.3	25.1	50.1
Mono-cyclohexyl phthalate							
µg/L of urine	2541	NC	<LOD	<LOD	<LOD	<LOD	<LOD
µg/g of creatinine*	2541	NC	<LOD	<LOD	<LOD	<LOD	<LOD
Mono-2-ethylhexyl phthalate							
µg/L of urine	2541	3.4	<LOD	1.2	3.2	7.6	14.8
µg/g of creatinine*	2541	3.1	<LOD	1.5	3.1	5.9	10.8
Mono-n-octyl phthalate							
µg/L of urine	2541	NC	<LOD	<LOD	<LOD	<LOD	1.6
µg/g of creatinine*	2541	NC	<LOD	<LOD	<LOD	<LOD	2.4

Mono-isononyl phthalate							
µg/L of urine	2541	NC	<LOD	<LOD	<LOD	<LOD	<LOD
µg/g of creatinine*	2541	NC	<LOD	<LOD	<LOD	<LOD	<LOD

* µg per gram of creatinine in urine

<LOD= Less than the limit of detection of the analytical method.

NC= Not calculated – Proportion of results below limit of detection was too high to provide a valid result.

Source: Centers for Disease Control and Prevention. Second National Report on Human Exposure to Environmental Chemicals. January 2003. (Accessed November 21, 2004)

<http://www.cdc.gov/exposurereport/2nd/pdf/secondner.pdf>

R.O.E. Indicator QA/QC

Data Set Name: PHTHALATE EXPOSURE

Indicator Number: 347 (89743)

Data Set Source: CDC, NHANES

Data Collection Date: ongoing

Data Collection Frequency: 2 year cycle

Data Set Description: Phthalate exposure

Primary ROE Question: What are the trends in biomeasures of exposure to common environmental pollutants including across population subgroups and geographic regions?

Question/Response

T1Q1 Are the physical, chemical, or biological measurements upon which this indicator is based widely accepted as scientifically and technically valid?

Urine samples were collected and processed in accordance with the methods indicated in the NHANES Specimen Collection and Laboratory/Medical Technologists Procedures Manual (LPM). See: <http://www.cdc.gov/nchs/data/nhanes/blood.pdf>
<http://www.cdc.gov/nchs/data/nhanes/LAB1-6.pdf>

T1Q2 Is the sampling design and/or monitoring plan used to collect the data over time and space based on sound scientific principles?

Yes. NHANES is designed to provide statistically representative national averages. Starting with NHANES 1999, the survey is conducted annually. A subsample of participants aged six years and older in NHANES 1999-2000 were measured for urine levels of the phthalate metabolites. Subsamples were randomly selected within the specified age range to be a representative sample of the U.S. population. The measurements produced by NHANES for this indicator were used in the “Second National Report on Human Exposure to Environmental Chemicals” published by the National Center for Environmental Health in 2003.
<http://www.cdc.gov/exposurereport/2nd/pdf/secondner.pdf>

T1Q3 Is the conceptual model used to transform these measurements into an indicator widely accepted as a scientifically sound representation of the phenomenon it indicates?

Not applicable

T2Q1 To what extent is the indicator sampling design and monitoring plan appropriate for answering the relevant question in the ROE?

This indicator is based on a national probability-based sampling design and is deemed of sufficient quality for generalization to the nation. The samples for 1999-2000 were used for this analysis. Quality assurance measures were in place. Beginning in 1999, NHANES became a continuous and annual survey. The sampling plan for each year follows a complex, stratified, multistage, probability-cluster design to select a representative sample of the civilian, noninstitutionalized population. The 1999 NHANES was conducted in 12 counties across the U.S. From these locations, 5,325 people were selected to participate in the survey. Of these, 3,812 (71%) participated in the examination component. Data collection ended in 2000.

T2Q2 To what extent does the sampling design represent sensitive populations or ecosystems?
The current sampling design includes oversampling of African Americans, Mexican Americans, adolescents (12-19 year olds), older Americans (60 years of age and older), and pregnant women to produce more reliable estimates for these groups.

T2Q3 Are there established reference points, thresholds or ranges of values for this indicator that unambiguously reflect the state of the environment?

This indicator simply provides information that exposure to a phthalate metabolite has occurred. Generally recognized guidelines for urinary levels of these phthalate metabolites have not been established. Measurements of urinary phthalate metabolites provide an estimate of exposure to various classes of phthalates. Furthermore, finding a measurable amount of one or more metabolites in urine does not by itself mean that the chemical has caused or will cause harmful effects. More research is needed to identify at which levels urinary phthalate metabolites constitute a health concern. As reported in "Second National Report on Human Exposure to Environmental Chemicals" published by the National Center for Environmental Health in 2003. <http://www.cdc.gov/exposurereport/2nd/pdf/secondner.pdf>

T3Q1 What documentation clearly and completely describes the underlying sampling and analytical procedures used?

Documentation for NHANES 1999-2000 is found on NCHS/CDC website at the following URL: http://www.cdc.gov/nchs/about/major/nhanes/nhanes99_00.htm#Laboratory%20Files The following provides more specific examples: The Addendum to the NHANES III for the 1999-2000 dataset clearly outlines the 1999-2000 sampling design and recommends analytic procedures. <http://www.cdc.gov/nchs/data/nhanes/guidelines1.pdf> <http://www.cdc.gov/nchs/data/nhanes/nhanes3/nh3gui.pdf> The "Second National Report on Human Exposure to Environmental Chemicals" published by the National Center for Environmental Health in 2003 more generally describes the NHANES 1999-2000 sampling plan. <http://www.cdc.gov/exposurereport/2nd/pdf/secondner.pdf> The NHANES 1999-2000 subsampling webpage clearly describes the subsampling methods used and how subsampled data should be analyzed <http://www.cdc.gov/nchs/about/major/nhanes/subsample.htm> as do the "Weighting Notes" posted on the NHANES website <http://www.cdc.gov/nchs/data/nhanes/frequency/weights%20to%20usev6.pdf>

T3Q2 Is the complete data set accessible, including metadata, data-dictionaries and embedded definitions or are there confidentiality issues that may limit accessibility to the complete data set?

For the most part, Individual level data are available, but data access limitations do exist for some variables due to confidentiality issues.

http://www.cdc.gov/nchs/about/major/nhanes/nhanes99_00.htm#Laboratory%20Files

T3Q3 Are the descriptions of the study or survey design clear, complete and sufficient to enable the study or survey to be reproduced?

Yes. The Addendum to the NHANES III for the 1999-2000 dataset clearly outlines the 1999-2000 sampling design and recommends analytic procedures.

<http://www.cdc.gov/nchs/data/nhanes/guidelines1.pdf>

<http://www.cdc.gov/nchs/data/nhanes/nhanes3/nh3gui.pdf>

T3Q4 To what extent are the procedures for quality assurance and quality control of the data documented and accessible?

The quality assurance plans for NHANES 1999-2000 are available from the Division of Data Dissemination, NCHS, 6525 Belcrest Rd. Hyattsville, MD, 20782-2003. Tel. 301-458-4636.

Internet: <http://www.cdc.gov/nchs/about/quality.htm>

T4Q1 Have appropriate statistical methods been used to generalize or portray data beyond the time or spatial locations where measurements were made (e.g., statistical survey inference, no generalization is possible)?

Yes. The NHANES 1999-2004 survey is designed to be annually nationally representative of the U.S. citizen, non-institutionalized population. (see page 11 of the addendum linked below)

<http://www.cdc.gov/nchs/data/nhanes/guidelines1.pdf>

T4Q2 Are uncertainty measurements or estimates available for the indicator and/or the underlying data set?

Yes. (see pages 11-19 of the addendum linked below)

<http://www.cdc.gov/nchs/data/nhanes/guidelines1.pdf>

T4Q3 Do the uncertainty and variability impact the conclusions that can be inferred from the data and the utility of the indicator?

NHANES selects a representative sample of the civilian, non-institutionalized population in the United States using a complex, stratified, multistage, probability-cluster design. Beginning in 1999, NHANES became a continuous and annual national survey. With only 2 years of data in NHANES 1999-2000, instead of the 6-years for NHANES III (1988-1994), some differences exist that may limit the underlying data with respect to completeness or representative of coverage. The sample size is smaller and the number of geographic units in the sample is more limited. The current 1999-2000 NHANES survey is nationally representative but it is subject to the limits of increased sampling error due to (1) the smaller number of individuals sampled in the annual sample and (2) the smaller number of Primary Sampling Units (PSUs) [see description below] available for each annual sample. Therefore, the sample size for any 1-year period is relatively small, possibly resulting in large variability for U.S. population estimates, especially those for narrowly defined demographic groups or other specific subgroup analyses. For NHANES 1999-2000, the first stage of selection was the PSU-level. The PSUs were defined as single counties. For a few PSUs, the county population was too small and those counties were

combined with geographically contiguous counties to form a PSU. The 1999-2000 NHANES sample is selected from a relatively small number of PSUs compared to NHANES III. With a small number of PSUs, variance estimates that account for the complex design may be relatively unstable, a factor which introduces a higher level of uncertainty in the annual estimates. NHANES is designed to increase precision by combining data across calendar years. Because of the relatively small sample size in 1999 and 2000, analytical data for just one or two survey participants may be weighted heavily and greatly influence the mean value reported. The number of geographic sites sampled each year is small and environmental exposures may vary geographically; thus producing environmental exposure estimates by geographic region using the NHANES data set is of limited value
<http://www.cdc.gov/nchs/about/major/nhanes/subsample.htm>

T4Q4 Are there limitations, or gaps in the data that may mislead a user about fundamental trends in the indicator over space or time period for which data are available?

As subsequent years are added to this survey, estimates will become more stable. However, with the laboratory data, there is no guarantee that an environmental chemical will be measured from year to year. It is unknown whether differences between ages, genders, or races/ethnicities represent differences in exposure, body-size relationships, or metabolism. Differences in the excretion of various phthalates may be due to differences in either exposure or toxicokinetics. The low detection rates for some of the long alkyl chain phthalates metabolites may be due to significantly less metabolism to the monoester metabolite. The measurement of an environmental chemical in a person's blood or urine does not by itself mean that the chemical has caused or will cause harmful effects.